

# THE UNITED STATES PATENT AND TRADEMARK OFFICE

#### CERTIFICATE OF MAILING

I hereby certify that this SECOND SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT and the documents referred to as enclosed therein are being deposited with the United States Postal Service on the date indicated below with sufficient postage as First Class Mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

Ariel Fletcher

Applicant: Brooks, et al.

Serial No.: 09/081,522

Filed: May 19, 1998

Title: INHIBITION OF ANGIOGENESIS
IN DISEASE STATES WITH AN
ANTI-α,β3 MONOCLONAL
ANTIBODY (AS AMENDED)

IN DISEASE STATED

Our Ref.: TSRI 419.0 Con 1

### SECOND SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Assistant Commissioner for Patents Washington, D.C. 20231

Dear Sir:

In recognition of their continuing duty to disclose pursuant to 37 CFR §1.56, Applicants hereby submit the present Supplemental Information Disclosure Statement and accompanying PTO Form 1449 in compliance therewith.

Applicants understand that the interpretation given to each reference may differ from one individual to another. The PTO is therefore encouraged to independently examine the disclosed references. While the references provided in this Supplemental

Information Disclosure Statement may be material pursuant to 37 CFR §1.56, it shall not be construed to be an admission that the cited information is, or is considered to be, material to patentability unless specifically designated as such.

Applicants are filing the present statement pursuant to 37 CFR §1.97(c). The statement is accompanied by a check in the amount of \$180.00 as payment of the fee set forth in 37 CFR §1.17(p) in accordance with 37 CFR §1.97(c)(2).

Also, in accordance with 37 CFR §1.97(g), the filing of this Supplemental Information Disclosure Statement shall not be construed to mean that a search has been made or, that if made, any search was complete or exhaustive, or that no other material information as defined in 37 CFR §1.56 exists.

Respectfully submitted,

Date

Emily Holmes, Reg. No. 40,65

THE SCRIPPS RESEARCH INSTITUTE
Office of Patent Counsel
10550 North Torrey Pines Road
Mail Drop TPC-8
La Jolla, CA 92037
(858) 784-2937

FORM TO 449 US DEPARTMENT OF PATENT AND TRADE	F COMMERCE MARK OFFICE		ATTY DOCKET NO. SERIAL NO. TSRI 419.0 C1 09/081,522  APPLICANT Brooks, et al.			SERIAL NO. 09/081,522
INFORMATION DISCOSURE STATEMENT BEIND LICANT			FILING DATE GROUP 05/19/98 1644			
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1 Christofanilli, et al., "A	ngiogenesis Modulation In Can	cer Research: Novel Clin	ical Approaches",	Nature Revi	ews 1: 415-4	26 (2002)
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EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

## By Hand Delivery

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicat	nt: Brooks, et al.	)
Serial N	o.: 09/081,522	) Group Art Unit: 1644
Filed:	May 19, 1998	) Examiner: P. Gambel
Γ.	NHIBITION OF ANGIOGENESIS N DISEASE STATES WITH AN NTI-ανβ3 MONOCLONAL NTIBODY (AS AMENDED)	) Confirmation No. 1607  Our Ref.: TSRI 419.0 Con 1

# THIRD SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. § 1.56 and § 1.97

Assistant Commissioner for Patents Washington, DC 20231

Sir:

In accordance with the continuing duty of disclosure imposed by 37 C.F.R. § 1.56 and § 1.97 to inform the Patent Office of all references coming to the attention of each individual associated with the filing or prosecution of the subject application, which are or may be material to the patentability of any claim of the application, Applicant hereby directs the Examiner's attention to the references listed on the attached revised form PTO-1449 entitled "List of References Cited by Applicant." A legible copy of the two attached references are being submitted herewith.

Identification of the listed references is not to be construed an admission of Applicant or Attorneys for Applicant that such references are available as "prior art" against the subject application.

Applicant respectfully requests that the Examiner review the foregoing references and that the references be made of record in the file history of the application.

Since this Supplemental Information Disclosure Statement is being filed before the mailing date of the first Office Action after the filing of a Request for Continued Examination under §1.114, the fee required to be filed with the accompanying Supplemental Information Disclosure Statement has been estimated to be \$0.00. However, should the Patent Office determine otherwise, please charge the required fee to Deposit Account No. 19-0962. A copy of this sheet is enclosed for accounting purposes.

Respectfully submitted,

September 16, 2003

Date

THE SCRIPPS RESEARCH INSTITUTE
Office of Patent Counsel
10550 North Torrey Pines Road
Mail Drop TPC-8
La Jolla, California 92037
(858) 784-2937
Enclosure

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LIST OF	REFI	ERENCES CITED B		CANT	APPLICANT				
		(Use several sheets if	necessary)		Brooks et al.				
				. •	FILING DATE 05/19/98		GROUP 1644		
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ATTY DOCKET NO.

APPLICATION NO

## EXAMINER

C03

DATE CONSIDERED

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

### IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

I hereby certify that this REQUEST and the documents referred to as enclosed therein are being deposited with the United States Postal Service on the date is First Class Mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450; Alexandria, VA 22313-Applicant: Brooks, et al. Serial No.: 09/081,522 Group Art Unit: 1644 Filed: May 19, 1998 Examiner: P. Gambel Title: INHIBITION OF ANGIOGENESIS IN DISEASE STATES WITH AN Confirmation No. 1607 ANTI-ανβ3 MONOCLONAL ANTIBODY (AS AMENDED) Our Ref.: TSRI 419.0 Con 1

# FOURTH SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. §1.56 and §1.97

In accordance with the continuing duty of disclosure imposed by 37 C.F.R. § 1.56 and § 1.97 to inform the Patent Office of all references coming to the attention of each individual associated with the filing or prosecution of the subject application, which are or may be material to the patentability of any claim of the application, Applicants hereby direct the Examiner's attention to the references listed on the attached revised form PTO-1449 entitled "List of References Cited by Applicant." A legible copy of the fifteen attached references are being submitted herewith.

Identification of the listed references is not to be construed an admission of Applicants or Attorneys for Applicants that such references are available as "prior art" against the subject application.

Applicants respectfully request that the Examiner review the foregoing references and that the references be made of record in the file history of the application.

Since this Supplemental Information Disclosure Statement is being filed before the mailing date of the first Office Action after the filing of a Request for Continued

Examination under §1.114, the fee required to be filed with the accompanying Supplemental Information Disclosure Statement has been estimated to be <u>\$0.00</u>. However, should the Patent Office determine otherwise, please charge the required fee to Deposit Account No. 19-0962. A copy of this sheet is enclosed for accounting purposes.

December 29, 2003

Date

THE SCRIPPS RESEARCH INSTITUTE Office of Patent Counsel 10550 North Torrey Pines Road Mail Drop TPC-8 La Jolla, California 92037 (858) 784-2937 Respectfully submitted,

Thomas Fitting, Reg. No. 34,163

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						TSRI 419.0 C1		09/081,522		
LIST OF	REFE	ERENCES CITED B	Y APPLICA	ANT		APPLICANT		<del></del>		
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	C01	Adams et al., "Increased	Affinity Lead	ls to Improv	ed Selecti	ve Tumor Delivery	of Single-(	Chain Fy An	tibodies."	
		Cancer Research 58: 485	5-490 (1998).							
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	C04	Cheresh et al., "Integrin-	mediated deat	h: An expla	nation of t	the integrin-knocko	ut phenoty	pe?" Nature	Medicine	<del></del>
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	C03	Metastatic Cancer," Can	cer Biotherapy	& Radioph	narmaceuti	icals 16: 125-132 (2	001).	•		
	C06	Rader et al., "Phage disp Proc. Natl. Acad. Sci. US	lay approach f	for rapid ant	ibody hun	nanization: Designe	d combina	torial V gene	e libraries,	,
	C07	Reynolds et al., "Enhance				e lacking β <sub>3</sub> integri	n or B <sub>2</sub> and	β <sub>s</sub> integrins	." Nature	
-		Medicine 8: 27-34 (2002	.).							
	C08 Schier et al., "Isolation of High-affinity Monomeric Human Anti-c-erbB-2 Single chain Fv Using affinity-driven Selection," J. Mol. Biol. 255: 28-43 (1996).							1		
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### IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

#### CERTIFICATE OF MAILING

I hereby certify that this INFORMATION DISCLOSURE STATEMENT and documents submitted therewith are being deposited with the United States Postal Service as first class mail, postage prepaid thereon, in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231, on the date indicated below.

Thomas Fitting, Reg. No. 34,163

Applicant: Brooks, et al.

Serial No.: 09/081,522

Filed: May 19, 1998

For: METHODS AND COMPOSITIONS

USEFUL FOR INHIBITION OF

ANGIOGENESIS

May 12,1999

Date

Date

May 12,1999

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## INFORMATION DISCLOSURE STATEMENT

Assistant Commissioner for Patents Washington, D.C. 20231

### Dear Sir:

In recognition of their continuing duty to disclose pursuant to 37 CFR 1.56, Applicants hereby submit the present Information Disclosure Statement and accompanying PTO Form 1449 in compliance therewith.

Applicants understand that the interpretation given to each reference may differ from one individual to another. The PTO is therefore encouraged to independently examine the disclosed references. While the references provided in this Information

Serial No.: 09/081,522 TSRI 419.0C1

Disclosure Statement may be material pursuant to 37 CFR 1.56, it shall not be construed to be an admission that the cited information is, or is considered to be, material to patentability unless specifically designated as such.

Applicants are filing the present statement pursuant to 37 CFR §1.97(b) insofar as this statement is being filed within three months of the filing of the application/before the mailing date of a first Office Action.

Also, in accordance with 37 CFR 1.97 (g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made or, that if made, any search was complete or exhaustive, or that no other material information as defined in 37 CFR 1.56 exists.

Respectfully submitted,

Dated: 3/12/95

Thomas Fitting, Reg. No. 34,163

THE SCRIPPS RESEARCH INSTITUTE Office of Patent Counsel 10550 North Torrey Pines Road Mail Drop TPC-8 La Jolla, CA 92037 (619) 784-2937

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EXAM. INITIALS	<u> </u>	DOCUMENT NUMBER	DATE	NAME		CLASS	SUB- CLASS	FILING DATE	
		5,092,885	3/3/92	U.S. Patent		<u> </u>			
,		5,112,946	5/12/92	U.S. Patent					
		5,192,744	3/9/93	U.S. Patent					
		5,202,352	4/13/93	U.S. Patent					
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		8905155	6/15/89	PCT					
		0 576 898 A2	6/15/93	European	Patent				
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		o	THER DOCUMENTS (	Including Author, Title, Da	te, Pertinent Pages)	)			
	1	Davis, et al., "Identification of Cell. Biochem. 51: 206-218 (1	Role of the Vitronectin				lial Cell Vasca	ılar Formation", <u>J. of</u>	
	2	Folkman, et al., "Angiogenic F	actors", <u>Science 235</u> : 44	2-447 (1987)					
	3	Moses, et al., "Identification of	an Inhibitor of Neovasc	ularization from Cartilage",	Science 248: 1408	-1410 (1990	)		
	4	Folkman, et al., "Inhibition of	Angiogenesis", Cancer B	<u>io. 3</u> : 89-96 (1992)					
	5	Blood, et al., "Turnor Interaction	ns with the Vasculature	Angiogenesis and Tumor I	Metastasis", <u>Biochi</u>	m. et Biophy	. Acta 1032: 8	9-118 (1990)	
	6	Ingber, et al., "Inhibition of An	giogenesis through Mod	ulation of Collagen Metabo	lism", <u>Lab. Invest.</u>	<u>59 (1)</u> : 44-51	(1988)		
-	7	Aumailley, et al., "Arg-Gly-As Fragment P1", Fed. of Euro, Bi	Constrained within Cy ochem. Soc. 291 (1): 50	clic Pentapeptides: Strong a -54 (1991)	nd Selective Inhibi	tors of Cell A	dhesion to Vit	ronectin and Laminin -	
	8	Choi, et al., "Inhibition of Neoi 125-134 (1994)	ntimal Hyperplasia by E	llocking $\alpha_s \beta_s$ Integrin with a	a Small Peptide An	tagonist Gpe	nGRGDSPCA	", <u>J. of Vasc. Surg. 19</u> :	
	9	Nicosia, et al., "Inhibition of As	ngiogenesis in vitro by A	rg-Gly-Asp-Containing Sy	nthetic Peptide", A	mer, Jour, of	Patho. 138 (4)	): 829-833 (1991)	
	10	Cheresh, et al., "Biosynthetic as Vitronectin, Fibrinogen, and vo	nd Functional Properties n Willebrand Factor", <u>J.</u>	of an Arg-Gly-Asp-directed of Bio. Chem. 262 (36): 17	d Receptor Involve 703-17711 (1987)	d in Human N	delanoma Cel	Attachment to	
	11	Leavesley, et al., "Integrin β1- 163-170 (1993)	and β3-mediated Endoth	elial Cell Migration is Trig	gered through Dist	inct Signalin	g Mechanisms	", <u>J. of Cell Biol. 121</u> :	
EXAMINER				DATE CONSI	DERED				

FORM PTO-14	49 U.S. DEPARTMENT OF CO PATENT AND TRADEMARK	MMERCE OFFICE			ATTY DOCKE TSRI 419.0			RIAL NO. 9/081,522
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12						cular Endothe	lial Cells", <u>J.</u>	of Inves. Derm. 99
13	Brooks, et al., "Subtractive Im	munization Yields Mone	oclonal Anti	bodies that Specif	ically Inhibit Meta	ıstasis", <u>J. of (</u>	Cell Biol. 122	<u>(6)</u> : 1351-1359
14	Nip, et al., "Human Melanoms 1406-1413 (1992)	Cells Derived from Ly	mphatic Me	tastases Use Integr	in α,β, to Adhere	to Lymph No	de Vitronecti	1", <u>J. Clin. Invest. 90</u> :
15	Jackson, et al., "Isolation and I 736 (1989)	ropagation of Endotheli	ial Cells De	rived from Rheum	atoid Synovial Mi	crovasculatur	e", <u>Ann. of th</u>	e Rheu. Dis. 48: 733-
16	Waldman, Thomas A., "Mono	lonal Antibodies in Dia	gnosis and	Therapy", Science	<u>252</u> : 1657-1662	(1991)		
17	Brooks, et al., "Requirement of			<del></del>		<del></del>		
18	Chuntharapai, et al., "Blocking Exper. Cell Res. 205: 345-352	Monoclonal Antibodies			<del></del>		esent on Hum	an Osteoclasts",
19	Osband, et al., "Problems in the	Investigational Study a	and Clinical	Use of Cancer Im	munotherapy", <u>In</u>	ım. Today 11	<u>(6)</u> : 193-19	(1990)
20	Ausprunk, et al., "Vascularizat	ion of Normal and Neor	olastic Tissu	es Grafted to the (	Chick Chorioallan	tois", <u>Amer.</u> J	, of Path, 79	<u>(3)</u> : 597-610 (1975)
EXAMINER				DATE CONSID				

FORM PTO-144	9 U.S. DEPARTMENT OF COM PATENT AND TRADEMARK			ATTY DOCKE TSRI 419.0 APPLICANT Brooks, et al.	Con 1		SERIAL NO. 09/081,522		
INFORMATION STATEMENT B				FILING DATE 5/19/98			GROUP 1648		
		U.S. I	PATENT DOCUMENTS						
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21	Cheresh, et al., "Recognition of (1989)				and Endothe	lial Cells", <u>Ce</u>	e <u>ll 58</u> : 945-953		
) 22	D'Amato, et al., "Thalidomide i	s an Inhibitor of Angiogo	enesis", Proc. Natl. Acad. S	<u>ci. USA 91</u> : 4082-	4085 (1994)		<del></del>		
23	Leibovich, et al., "Macrophage-	nduced Angiogenesis is	Mediated by Tumour Necr	osis Factor-α", <u>Na</u> t	ure 329.: 630	-632 (1987)			
24	Pfaff, et al., "Selective Recognit (32): 20233-20238 (1994)	ion of Cyclic RGD Pepti	des of NMR Defined Confo	ormation by αlibβ3	, and α5β1 I	ntegrins", <u>J. of</u>	Biol, Chem. 269		
25	Yan, et al., "Human/Severe Con Endothelial Cell-Leukocyte Adr	nbined Immunodeficient esion Molecules", <u>J. Cli</u>	Mouse Chimeras: An Expe n. Invest. 91: 986-996 (199	erimental in Vivo M	fodel System	to Study the I	Regulation of Human		
26	Gurrath, et al., "Conformation/A	ctivity Studies of Ration	nally Designed Potent Anti-	Adhesive RGD Pe	ptides", <u>Eur.</u>	I. Biochem 21	<u>0</u> : 911-921 (1992)		
27	Leven, et al., "Extracellular Mai Receptor", Exp. Hematol. 20: 13	rix Stimulation of Guine 116-1322 (1992)	ea Pig Megakaryocyte Prop	latelet Formation is	n vitro Is Mec	liated Throug	h the Vitronectin		
28	Lafrenie, et al., "Up-regulated B 2202-2208 (1992)	iosynthesis and Expressi	on of Endothelial Cell Vitro	onectin Receptor E	nhances Cano	er Cell Adhes	ion", Canc. Res. 52:		
29	Klein, et al., "Basic Fibroblast C (1993)	rowth Factor Modulates	Integrin Expression in Mic	rovascular Endoth	elial Cells", ]	Mol. Bio. of th	ne Cell 4: 973-982		
EXAMINER			DATE CONSID	DERED					

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

### CERTIFICATE OF MAILING

I hereby certify that this SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT and the documents referred to as enclosed therein are being deposited with the United States Postal Service on the date indicated below with sufficient postage as First Class Mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

Ariel Fletcher	0/10/200  Date of Deposit
Applicant: Brooks, et al.	)
Serial No.: 09/081,522	) Group Art Unit: 1644
Filed: May 19, 1998	) Examiner: P. Gambel
Title: INHIBITION OF ANGIOGENESIS IN DISEASE STATES WITH AN ANTI-α,β3 MONOCLONAL ANTIBODY (AS AMENDED)	) ) ) Our Ref.: TSRI 419.0 Con 1 ) )

# SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Assistant Commissioner for Patents Washington, D.C. 20231

Dear Sir:

In recognition of their continuing duty to disclose pursuant to 37 CFR §1.56, Applicants hereby submit the present Supplemental Information Disclosure Statement and accompanying PTO Form 1449 in compliance therewith.

Applicants understand that the interpretation given to each reference may differ from one individual to another. The PTO is therefore encouraged to independently examine the disclosed references. While the references provided in this Supplemental Information Disclosure Statement may be material pursuant to 37 CFR §1.56, it shall not be construed to be an admission that the cited information is, or is considered to be, material to patentability unless specifically designated as such.

Applicants are filing the present statement pursuant to 37 CFR §1.97(c). The statement is accompanied by a check in the amount of \$180.00 as payment of the fee set forth in 37 CFR §1.17(p) in accordance with 37 CFR §1.97(c)(2).

Also, in accordance with 37 CFR §1.97(g), the filing of this Supplemental Information Disclosure Statement shall not be construed to mean that a search has been made or, that if made, any search was complete or exhaustive, or that no other material information as defined in 37 CFR §1.56 exists.

Respectfully submitted,

Date 10, 2001

Emily Holmes, Reg. No. 40,652

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